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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/711,155	08/27/2004	Bryan E. GARNER	5233.012.NPUS00	5154

28694 7590 04/14/2006

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/711,155	GARNER, BRYAN E.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-36 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-36 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/27/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-36 have been examined herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-36 are indefinite over the recitation of the phrases "quantifying a presence" and "quantifying the presence". This phrase in considered indefinite because it is unclear whether "quantifying a presence" and "quantifying the presence" are intended to mean detecting the presence of the microorganism or if is intended to mean determining the quantity of the microorganism. In the later case, the claims recite only method steps which allow for the detection of the presence or absence of a microorganism. The claims do not clearly set forth how the detection of the presence or absence of a microorganism allows for the determination of the quantity of the microorganism.

Claim 19 is indefinite over the recitation of the phrase "good number". This phrase in considered unclear because "good number" is not clearly defined in the specification and there is no art recognized definition for this phrase. For example, it is unclear as to whether a "good number" is 1, 2, 5, or 10.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7-8, 13, 15, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomas (Applied and Environmental Microbiology).

Thomas et al teach a method comprising: (a) culturing a sample under conditions suitable for growth; (b) using at least one oligonucleotide to detect the presence or absence of the specific kind of microorganism in respective portions of the cultured sample; and (c) quantifying the presence of the specific kind of microorganism in the sample of material from the detected presence or absence of the specific kind of microorganism in the respective portions of the cultured sample. Specifically Thomas et al teach a method wherein samples were cultured, followed by DNA extraction and species-specific detection of the organism using PCR and gel electrophoresis (Abstract). The protocol followed by Thomas for PCR requires the use of complementary oligonucleotide primers which bind to the sample in order to amplify the

DNA prior to detection. In the instant case "quantifying" is being interpreted by determining if the sample is present or absent based on the presence or absence of a specific band on the gel. The sample can be quantified based on the strength of the band wherein a darker band means more Listeria monocytogenes is present, a lighter band means less Listeria monocytogenes is present, and no band means that no Listeria monocytogenes is present. Also milk and beef can be used to feed animals.

Regarding Claim 7, Thomas et al teach a method wherein at least one oligonucleotide hybridizes with a nucleic acid sequence that is indicative of a species of the specific kind of microorganism. Specifically Thomas et al teach that five different combinations of complementary oligonucleotide primers were used to amplify the DNA prior to detection (Abstract). The oligonucleotide primers hybridize to the nucleic acid sequence that is being detected and serve as a starting point for DNA amplification.

Regarding Claim 8, Thomas et al teach a method wherein the sample is cultured on a plate of culture media, and the respective portions of the cultured sample are taken from respective colonies of microorganisms that have been found to have grown on the plate of culture media. Specifically Thomas et al teach that skim milk and ground beef were inoculated with L. monocytogenes. Next the milk samples and beef samples were mixed with Listeria enrichment broth and aliquots of each mixture were plated onto LPM agar plates. The plates were grown overnight and in the morning DNA was extracted from the colonies grown on the plates (Page 2577).

Regarding Claim 13, Thomas et al teach a method wherein two oligonucleotide primers are used to induce a polymerase chain reaction in the presence of nuclear

material of the specific kind of microorganism, and detecting the presence or absence of a product of the polymerase chain reaction. Specifically Thomas et al teach a method wherein samples are amplified using PCR and the PCR products were detected using gel electrophoresis (Abstract). The protocol followed by Thomas for PCR requires the use of 5 combinations of complementary oligonucleotide primers which bind to the sample in order to amplify the DNA (Abstract). Each combination includes a forward and reverse primer.

Regarding Claim 15, Thomas et al teach a method wherein the detecting of the presence or absence of a product includes performing electrophoresis of the polymerase chain reaction products to detect a reaction product having a characteristic molecular length indicative of a specific kind of microorganism. Specifically Thomas et al teach that the PCR products were analyzed using gel electrophoresis. The 520 bp band is indicative of the presence of L. monocytogenes (Figure 2).

Regarding Claim 17, Thomas et al teach a method comprising: (a) dividing the sample into multiple portions; (b) culturing each portion of the sample; (c) performing a polymerase chain reaction using two oligonucleotide primers; (d) detecting the presence or absence of a reaction product having a characteristic length; and (e) quantifying the presence of the specific kind of microorganism. Specifically Thomas et al teach a method wherein milk samples inoculated with different amounts of L. monocytogenes and cultured, followed by DNA extraction and species specific detection of the organism using PCR (utilizing a forward and reverse primer) and gel electrophoresis (Abstract). In the instant case "quantifying" is being interpreted by determining if the sample is

present or absent based on the presence or absence of a specific band on the gel. The sample can be quantified based on the strength of the band wherein a darker band means more Listeria monocytogenes is present, a lighter band means less Listeria monocytogenes is present, and no band means that no Listeria monocytogenes is present.

Regarding Claim 19, Thomas et al teach a method wherein the sample is diluted prior to the culturing of the portions of the sample so that a good number of the cultured portions of the sample have an absence of a reaction product having the characteristic length. Specifically Thomas et al teach that milk samples were inoculated with a different amount of L. monocytogenes (i.e. 2.5×10^6, 2.5×10^5, 2.5×10^4, etc.) and cultured overnight. PCR was performed on each milk sample to detect the presence of absence of L. monocytogenes in the sample. The results are shown in Figure 4. For the samples that were cultured in LEB24 (listeria enrichment broth 24 hours), L. monocytogenes was not present in milk samples inoculated with 2.5, 0.25, and 0 CFU of L. monocytogenes. For the samples that were cultured in LEB24 (listeria enrichment broth 24 hours) and plated on LPM (listeria plating medium), L. monocytogenes was not present in milk samples inoculated with 0.25, and 0 CFU of L. monocytogenes. In the instant case "good number" is being interpreted as at least two, therefore the teachings of Thomas et al meet the limitation of a "good number" for this claim.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, 21-22, 24-28, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware (US Patent 5534271).

The teachings of Thomas et al are presented above.

Regarding Claims 2-3, and 26 Thomas et al do not teach that the sample of animal feed was taken from a feedpile and transported to a testing lab in way so that the sample at the lab is representative of the condition of the animal feed when the animal feed is to be consumed by animals. Additionally Thomas et al do not teach that the sample of animal feed is taken from a feedpile at a location where the animal feed is to be consumed by animals.

However, Ware et al teaches a method wherein steer food containing L. acidophilus is tested. The test samples were taken from steer food and the testing was done to determine the amount of L. acidophilus in the samples. The testing was performed at the Silliker Laboratories in Chicago, IL (Column 11). Ware et al does not exemplify that the samples are taken from a feedpile at a location where the animal feed is to be consumed, however it would be obvious to one of ordinary skill in the art at the

time the invention was made to have tested the sample under the same conditions of the animal feed when it is feed to animals because Ware et al teaches that L acidophilus is a very sensitive organism that is difficult to maintain in a viable state at ambient temperatures. Any shift in the temperature during the transportation of the sample from the animal feedlot to the laboratory could potentially kill the L. acidophillus during transportation thus yeilding invalid results.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to taken a sample of animal feed to a laboratory in order to perform testing for the added benefit of providing a sterile testing facility. Both Microbiology and Molecular biology assays are very sensitive and can be contaminated easily. By performing the assay in a FDA laboratory, steps are taken to ensure that contamination does not occur.

Regarding Claims 4-5, Thomas et al do not teach a method wherein the specific kind of probiotic microorganism is Lactobacillus or L. acidophilus.

However Ware et al teach a method for detecting Lactobacillus acidophilus found in animal feed (Column 11).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and quantify Lactobacillus or L. acidophilus. This genus and species are routinely added to animal feed to increase milk and meat production. It would be benefical to quantitate the amount of L. acidophilus is animal feed because Ware et al have shown that the

amount of the probiotic in animal feed can change depending on the storage conditions (Column 11 and 12).

Regarding Claim 25 Thomas et al teach a method of contacting food (i.e. milk or meat) with a microorganism (Listeria), culturing the sample and then detecting the microorganism using PCR and gel electrophoresis. Thomas et al do not exemplify the above method wherein the food is animal feed and the microorganism is a probiotic microorganism.

However, Ware et al teach a method wherein probiotic bacteria cultures (i.e. Lactobacillus acidophilus) are mixed with an animal feedlot diet consisting of corn, dried gain, alfalfa, and corn meal and detected (Column 4 and 11).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have detected probiotic bacteria cultures mixed with an animal feedlot for the benefit of providing a method which can be used to assay for the amount of organisms present in animal feed. Probiotics are routinely added to animal feed to increase milk and meat production. It would be benefical to quantitate the amount of probiotics in animal feed because Ware et al have shown that the amount of the probiotic in animal feed can change depending on the storage conditions (Column 11 and 12).

Regarding Claims 27-28, Ware teaches that the probiotic being mixed with the animal feed and being detected is Lactobacillus acidophilus (Column 2 and Column 11).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and

quantify Lactobacillus and L. acidophilus in animal feed because these microorganisms are routinely added to animal feed to increase milk and meat production.

5. Claims 6 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware and further in view of Rust et al (Cattle Call).

The teachings of Thomas et al and Ware are presented above.

Thomas et al and Ware do not teach that the specific organism being detected in the animal feed is Lactobacillus LA-51.

However Rust et al teach that strain LA51 of Lactobacillus acidophilus can be added to animal feed. The addition of LA51 has been shown to help improve carcass adjusted average daily gain and feed conversion efficiency (Summary).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Thomas et al to detect and quantify Lactobacillus LA51 in animal feed because it is an important micororganism that is routinely added to animal feed to improve carcass adjusted average daily gain and feed conversion efficiency.

6. Claims 9-11, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Pahuski (US Patent 5587286).

The teachings of Thomas et al are presented above.

Regarding Claims 9, Thomas et al do not teach a method wherein the sample is cultured by dividing the sample into multiple portions and culturing each portion.

However, Pahuski et al teach a method for detecting the amount of organisms in milk. The test sample contains 10 µl of S. liquefaciens in 1 ml of milk. The sample is divided into 11 different test tubes. The test tubes are then plated and allowed to grow overnight (Column 15).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have divided the test sample into multiple portions and cultured each portion for the added benefit of having multiple samples to test which can be used to further confirm the results.

Regarding Claim 10, Thomas et al do not teach a method wherein the sample is divided into the multiple portions by diluting the sample and dividing the diluted sample into the multiple portions.

However, Pahuski et al teach a method for detecting the amount of organisms in milk. The test sample contains 10 µl of S. liquefaciens in 1 ml of milk. The sample is divided into 11 different test tubes, and each test tube has a different amount of the test sample ranging from 0-1000 µl and a different amount of pasteurized milk ranging from 0-1000 µl. The test tubes are then serially diluted and then each dilution is plated and allowed to grow overnight (Column 15).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have

divided the test sample into multiple portions by diluting the sample and dividing the diluted sample into multiple portions for the added benefit of having multiple samples containing all different amounts of bacteria to test which can be used to further confirm the results and obtain information on the specificity of the assay.

Regarding Claim 11, Thomas et al teach a method wherein the sample is divided into multiple portions by mixing the sample with liquid to produce a fluid mixture, and dividing the fluid mixture into the multiple portions.

However, Pahuski et al teach that the sample is divided into 11 different test tubes, and each test tube has a different amount of the test sample ranging from 0-1000 µl and a different amount of pasteurized milk (which is a liquid) ranging from 0-1000 µl. The test tubes are then serially diluted and each dilution is plated and allowed to grow overnight (Column 15).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have divided the test sample into multiple portions by mixing with a liquid because this is an effective method of creating multiple portions containing the bacteria. The benefit of having multiple samples to test is that they can be used to further confirm the results and obtain information on the specificity of the assay.

Regarding Claim 17, Thomas et al do not teach that the samples are divided into multiple portions prior to culturing.

However, Pahuski et al teach a method for detecting the amount of organisms in milk. The test sample contains 10 µl of S. liquefaciens in 1 ml of milk. The sample is

divided into 11 different test tubes. The test tubes are then plated and allowed to grow overnight (Column 15).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have divided the test sample into multiple portions (either by diluting or mixing with a liquid) and cultured each portion for the added benefit of having multiple samples to test which can be used to further confirm the results.

Regarding Claim 19 Thomas et al do not exemplify that the sample is diluted prior to culturing so that a good number of cultured portions have an absence of a reaction product having the charactersitic length. However Thomas does exemplify that different dilutions can be run on the gel in order to determine the sensitivity of the reaction. As shown by Thomas the lowest two dilutions do not have bands (Figure 4).

However, Pahuski et al teaches that the test sample contains 10 µl of S. liquefaciens in 1 ml of milk. The sample is divided into 11 different test tubes, and each test tube has a different amount of the test sample ranging from 0-1000 µl and a different amount of pasteurized milk ranging from 0-1000 µl. The test tubes are then serially diluted and then each dilution is plated and allowed to grow overnight (Column 15).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have diluted the test sample into multiple portions (either by diluting or mixing with a liquid) and cultured each portion to determine the sensitivity of the reaction.

7. Claims 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Lucchini (Federation of European Microbiological Societies).

Regarding Claim 12 Thomas et al do not teach a method wherein one oligonucleotide is used to detect the presence or absence of the specific kind of microorganism by detecting the hybridization of the oligonucleotide with sample nucleic acid sequence.

However, Lucchini et al teach a method wherein labeled oligonucleotide probe is hybridized with a sample population in order to quantitate the number of microorganisms in the sample population. Sample DNA was spotted onto a nylon membrane and allowed to hybridize over night with a labeled probe. The nylon membrane was then subjected to chemiluminescent detection and the hybridization was visualized by exposure on X ray film. The probe used was a 1150-bp fragment of the apf gene that was PCR labeled with a digoxigenin-11-dUTP (Page 275).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have used a labeled oligonucleotide probe capable of hybridizing to the sample DNA in order to detect the presence/absence of a specific microorganism. The benefit of using a labeled probe to detect a specific microorganism is that it simplifies traditional methods of obtaining a total viable count by counting.

Regarding Claims 14 Thomas et al do not teach a method wherein one PCR primer hybridizes with a nucleic acid sequence indicative of the genus of the specific kind of microorganism, and another of the PCR primers hybridizes with a nucleic acid sequence indicative of the species of the specific kind of microorganism.

However Lucchini et al teach that multiplex PCR was performed using four oligonucleotide primers. Two genus specific primers named LARNA5 and LARNA6 were used. These primers were specific to a conserved region of 248 bp within the 16S rRNA gene of lactobacilli. Two species-specific primers named APF3 and APF4 were also used. These primers were specific to L. gasseri.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have used one PCR primer which hybridizes with a nucleic acid sequence indicative of the genus of the specific kind of microorganism, and another of the PCR primers hybridizes with a nucleic acid sequence indicative of the species of the specific kind of microorganism for the added benefit of being able to distinguish between different species when more than one species is suspected of being present in the sample to be tested.

8. Claims 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Wang (Applied and Environmental Microbiology).

The teachings of Thomas et al are presented above.

Regarding Claim 16 Thomas et al do not exemplify a method wherein the presence of the specific kind of microorganism in the sample of material is quantified in terms of a most probable number of the specific kind of microorganism.

However Wang et al teach a method for PCR detection and quantitation of microorganisms. Wang et al quantitated 12 bacterial species in human and animal fecal samples by PCR (Table 3). Quantitation was done by diluting samples down, running the samples on a gel, and comparing the band strength to various controls. This method was used to determine the probable number of microorganisms.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to quantified the amount of microorganisms in the sample using the method of Wang. The method taught by Wang et al is a simple PCR based method that could be helpful for studies on the role of intestinal bacteria in xenobiotic metabolism and in safety evaluation of various food additives. The benefits of using the method of Wang are that it is fast and can provide specific detection and quantitation of a wide range of bacterial species, thus improving the overall evaluation and characterization of the sample.

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Pahuski (US Patent 5587286) and in further view of Wang (Applied and Environmental Microbiology).

The teachings of Thomas et al and Pahuski et al are presented above.

Regarding Claim 18 the combined references do not exemplify a method wherein the presence of the specific kind of microorganism in the sample of material is quantified in terms of a most probable number of the specific kind of microorganism.

However Wang et al teach a method for PCR detection and quantitation of microorganisms. Wang et al quantitated 12 bacterial species in human and animal fecal samples by PCR (Table 3). Quantitation was done by diluting samples down, running the samples on a gel, and comparing the band strength to various controls. This method was used to determine the probable number of microorganisms.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to quantified the amount of microorganisms in the sample using the method of Wang. The method taught by Wang et al is a simple PCR based method that could be helpful for studies on the role of intestinal bacteria in xenobiotic metabolism and in safety evaluation of various food additives. The benefits of using the method of Wang are that it is fast and can provide specific detection and quantitation of a wide range of bacterial species, thus improving the overall evaluation and characterization of the sample.

10. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Pahuski (US Patent 5587286) and in further view of Lucchini (Federation of European Microbiological Societies).

The teachings of Thomas et al and Pahuski et al are presented above.

Regarding Claim 20 the combined references do not teach a method wherein one PCR primer hybridizes with a nucleic acid sequence indicative of the genus of the specific kind of microorganism, and another of the PCR primers hybridizes with a nucleic acid sequence indicative of the species of the specific kind of microorganism.

However Lucchini et al teach that multiplex PCR was performed using four oligonucleotide primers. Two genus specific primers named LARNA5 and LARNA6 were used. These primers were specific to a conserved region of 248 bp within the 16S rRNA gene of lactobacilli. Two species-specific primers named APF3 and APF4 were also used. These primers were specific to L. gasseri.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have used one PCR primer which hybridizes with a nucleic acid sequence indicative of the genus of the specific kind of microorganism, and another of the PCR primers hybridizes with a nucleic acid sequence indicative of the species of the specific kind of microorganism for the added benefit of being able to distinguish between different species when more than one species is suspected of being present in the sample to be tested.

11. Claims 21-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Pahuski (US Patent 5587286) and in further view of Ware (US Patent 5534271).

The teachings of Thomas et al and Pahuski et al are presented above.

Regarding Claims 21 and 22 the combined references do not teach that the specific microorganism being detected is Lactobacillus or L. acidophilus.

However Ware et al teach a method for detecting Lactobacillus acidophilus found in animal feed (Column 11).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and quantify Lactobacillus or L. acidophilus. This genus and species are routinely added to animal feed to increase milk and meat production. It would be benefical to quantitate the amount of L. acidophilus is animal feed because Ware et al have shown that the amount of the probiotic in animal feed can change depending on the storage conditions (Column 11 and 12).

Regarding Claim 24 the combined references do not teach that the sample of the sample of animal feed from a feedpile at a location where the animal feed is to be consumed by animals.

However, Ware et al teaches a method wherein steer food containing L. acidophilus is tested. The test samples were taken from steer food and the testing was done to determine the amount of L. acidophilus in the samples. The testing was performed at the Silliker Laboratories in Chicago, IL (Column 11). Ware et al does not exemplify that the samples are taken from a feedpile at a location where the animal feed is to be consumed, however it would be obvious to test the sample under the same conditions of the animal feed when it is feed to animals because Ware et al teaches that L acidophilus is a very senstive organism that is difficult to maintain in a viable state at

ambient temperatures. Any shift in the temperature during the transportation of the sample from the animal feedlot to the laboratory could potentially kill the L. acidophillus during transportation thus yeilding invalid results.

12. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Pahuski (US Patent 5587286) and Ware and in further view of Rust et al (Cattle Call).

The teachings of Thomas et al, Pahuski and Ware are presented above.

The combined references do not teach that the specific organism being detected in the animal feed is Lactobacillus LA-51.

However Rust et al teach that strain LA51 of Lactobacillus acidophilus can be added to animal feed. The addition of LA51 has been shown to help improve carcass adjusted average daily gain and feed conversion efficiency.

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and quantify Lactobacillus LA51 in animal feed because it is an important micororganism that is routinely added to animal feed to improve carcass adjusted average daily gain and feed conversion efficiency.

13. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware (US Patent 5534271) and in further view of Wang (Applied and Environmental Microbiology).

The teachings of Thomas et al and Ware et al are presented above.

The combined references do not teach a method wherein the presence of the microorganism in the sample of material is quantified in terms of a most probable number of the microorganism.

However Wang et al teach a method for PCR detection and quantitation of microorganisms found in human and animal fecal samples. Wang et al quantitated 12 bacterial species in human and animal fecal samples by PCR (Table 3). Quantitation was done by diluting samples down, running the samples on a gel, and comparing the band strength to various controls. This method was used to determine the probable number of microorganisms.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to quantified the amount of microorganisms in the sample using the method of Wang. The method taught by Wang et al is a simple PCR based method that could be helpful for studies on the role of intestinal bacteria in xenobiotic metabolism and in safety evaluation of various food additives. The benefits of using the method of Wang are that it is fast and can provide specific detection and quantitation of a wide range of bacterial species, thus improving the overall evaluation and characterization of the sample.

14. Claims 31, and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware (US Patent

5534271) and in further view of Lucchini (Federation of European Microbiological Societies).

The teachings of Thomas et al and Ware are presented above.

Regarding Claim 31 the combined references do not teach a method wherein one oligonucleotide is used to detect the presence or absence of the specific kind of microorganism by detecting the hybridization of the oligonucleotide with sample nucleic acid sequence.

However, Lucchini et al teach a method wherein labeled oligonucleotide probe is hybridized with a sample population in order to quantitate the number of microorganisms in the sample population. Sample DNA was spotted onto a nylon membrane and allowed to hybridize over night with a labeled probe. The nylon membrane was then subjected to chemiluminescent detection and the hybridization was visualized by exposure on X ray film. The probe used was a 1150-bp fragment of the apf gene that was PCR labeled with a digoxigenin-11-dUTP (Page 275).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to have used a labeled oligonucleotide probe capable of hybridizing to the sample DNA in order to detect the presence/absence of a specific microorganism. The benefit of using a labeled probe to detect a specific microorganism is that it simplifies traditional methods of obtaining a total viable count by counting.

Regarding Claims 33-34, Ware teaches that the probiotic being mixed with the animal feed is Lactobacillus acidophilus (Column 2).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and quantify Lactobacillus and L. acidophilus in animal feed because these microorganisms are routinely added to animal feed to increase milk and meat production.

15. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware (US Patent 5534271) in view of Lucchini (Federation of European Microbiological Societies) in further view of Rust et al (Cattle Call).

The teachings of Thomas et al, Ware et al, and Lucchini et al are presented above.

The combined references do not teach that the specific organism being detected in the animal feed is Lactobacillus LA-51.

However Rust et al teach that strain LA51 of Lactobacillus acidophilus can be added to animal feed. The addition of LA51 has been shown to help improve carcass adjusted average daily gain and feed conversion efficiency (Summary).

Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al to detect and quantify Lactobacillus LA51 in animal feed because it is an important micororganism that is routinely added to animal feed to improve carcass adjusted average daily gain and feed conversion efficiency.

16. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas (Applied and Environmental Microbiology) in view of Ware (US Patent 5534271) in further view of Lucchini (Federation of European Microbiological Societies) and in further view of Wang (Applied and Environmental Microbiology).

The teachings of Thomas et al, Ware et al, and Lucchini et al are presented above.

The combined references do not teach a method wherein the presence of the microorganism in the sample of material is quantified in terms of a most probable number of the microorganism.

However Wang et al teach a method for PCR detection and quantitation of microorganisms found in human and animal fecal samples. Wang et al quantitated 12 bacterial species in human and animal fecal samples by PCR (Table 3). Quantitation was done by diluting samples down, running the samples on a gel, and comparing the band strength to various controls. This method was used to determine the probable number of microorganisms.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Thomas et al so as to quantified the amount of microorganisms in the sample using the method of Wang. The method taught by Wang et al is a simple PCR based method that could be helpful for studies on the role of intestinal bacteria in xenobiotic metabolism and in safety evaluation of various food additives. The benefits of using the method of Wang are that

it is fast and can provide specific detection and quantitation of a wide range of bacterial species, thus improving the overall evaluation and characterization of the sample.

Double Patenting

17. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1 and 7-20 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-15 of copending Application No. 10/711156. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-6 and 21-36 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/711,156 in view of Ware. Although the conflicting claims are not identical, they are not patentably distinct from each other. Both the present claims and the claims of '156 encompass methods for quantifying the presence of a microorganism in a sample of animal feed using at least one oligonucleotide. The present claims differ from the claims of '156 in that the claims of '156 do not recite that the micororgansim being detected is Lactobacillus, L. acidophilus, or Lactobacillus LA51 in samples of animal feed that are transported from an animal feedlot to a laboratory for culturing and using an oligonucleotide to detect the microorganism. However, Ware teaches a method for detecting L. acidophilus in steer food. The test samples were taken from steer food and the testing was performed at the Silliker Laboratories in Chicago, IL (Column 11). Ware et al does not exemplify that the samples are taken from a feedpile at a location where the animal feed is to be consumed, however it would be obvious to one of ordinary skill in the art at the time the invention was made to have tested the sample under the same conditions of the animal feed when it is feed to animals because Ware et al teaches that L acidophilus is a very sensitive organism that is difficult to maintain in a viable state at ambient temperatures. Any shift in the temperature during the transportation of the sample from the animal feedlot to the

laboratory could potentially kill the L. acidophillus during transportation thus yeilding invalid results. Additionally Rust et al teach that strain LA51 of Lactobacillus acidophilus can be added to animal feed. The addition of LA51 has been shown to help improve carcass adjusted average daily gain and feed conversion efficiency (Summary). Accordingly it would have been obvious to one of ordinary skill in the art at the time the invention was made to detect and quantify Lactobacillus LA51 in animal feed because it is an important micororganism that is routinely added to animal feed to improve carcass adjusted average daily gain and feed conversion efficiency.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634
April 12, 2006

CARLA J. MYERS
PRIMARY EXAMINER